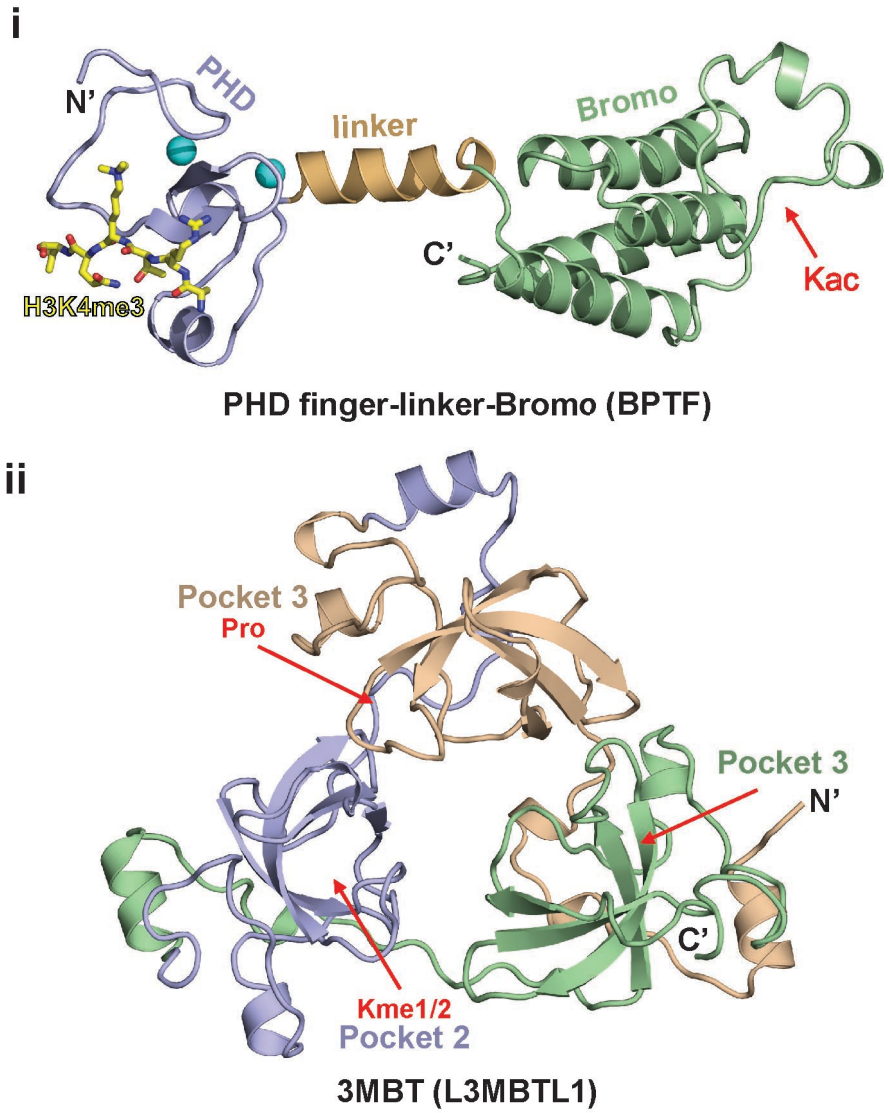
Supplementary figure S1



Supplementary Box 1. Protein scaffolds containing two or more reader modules precisely positioned for multivalent recognition.

(a) BPTF PHD finger-linker-bromodomain

The PHD finger and bromodomains are separated by an α-helical linker in the crystal crystal structure of the BPTF PHD finger-linker-bromodomain (panel i)[1]. The linker acts as a spacer, and in addition orients the binding pockets of the two reader modules. A structure was also solved of the BPTF PHD finger-linker-bromodomain with bound H3K4me3-containg peptide, where Kme3 is inserted into an aromatic cage in the PHD finger (panel i).

(b) L3MBTL1: A triangular scaffold composed of three MBT repeats, each with its own binding pocket

The L3MBTL1 protein with its three reader modules positioned on the same face of the protein (panel ii) can potentially participate in combinatorial readout of two or more marks[34]. Thus, histone peptides containing proline in a Pro-Ser context separated by an appropriate distance from a Kme mark could simultaneously target pockets 1 and 2 on L3MBTL1, a constraint potentially satisfied by Pro30 and methylated K36/37 in histone H3.3.

[1]Li, H. et al. Molecular basis for site-specific read-out of histone H3K4me3 by the BPTF PHD finger of NURF. *Nature* **442**, 91-5 (2006).